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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

YAEN, CHRISTOPHER H

ART UNIT

PAPER NUMBER

1643

DATE MAILED: 03/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/067,482

Applicant(s)

SUN ET AL.

Examiner

Christopher H. Yaen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6,15 and 17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6,15 and 17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

Re: Sun *et al*

1. The amendment filed 2/14/2006 is acknowledged and entered into the record. Accordingly, claims 1-5, 7-14,16, and 18-27 are canceled without prejudice or disclaimer.
2. Claims 6,15, and 17 are pending and examined on the merits.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Maintained/Re-Instated - 35 USC § 101 and

35 USC § 112, 1st paragraph

4. Upon further review and reconsideration, the rejection of claims 6,15, and 17 under 35 USC 101 as lacking a substantial and specific well established utility is maintained for the reasons of record. In the response filed 1/14/2005, applicant argues that the instantly claimed invention satisfied the utility requirements. Specifically, applicant argues that the examiner has not provided any basis for doubting the assertion that the claims polypeptide could be used as a marker for angiogenesis. These arguments have been carefully considered but are not deemed persuasive. In the office action mailed 3/5/2004 and 10/21/2004, a *prime facie* case was made that has established that the correlation between nucleic acids expression levels and protein expression levels are not always directly correlative. Applicant has not provided any objective evidence to indicate that such is not true for the instantly claimed polypeptide.

Applicant also argues that the polypeptide has utility because it can be used as a marker for expression for the nucleic acid coding for it, and if expressed can be used to determine those cells that expressed it (see page 8, response filed 1/14/2005) These arguments have been carefully considered but are not deemed persuasive. The requirement for utility indicates that a utility must be specific and substantial. In this case, the proposed utility is a general utility that can be applied to a general class of proteins and therefore not deemed specific. Any nucleic acid when transfected into a cell can be expressed and would be indication that the nucleic acid is present and therefore expressed. Therefore, it is not a specific utility. Applicant additionally argues that a declaration provided by Dr. Sun establishes the up-regulation of ANH401 mRNA and thus would confer utility to the protein, which it encodes. These arguments have been carefully considered but are not persuasive. First, the declaration provided by Dr. Sun is not signed and is therefore not a valid declaration. Secondly, the declaration submitted is not commensurate in scope. The claims are drawn to a polypeptide of SEQ ID No: 2 and methods of using the polypeptide, while the declaration provided is drawn to nucleic acids and methods of detecting nucleic acids.

Therefore, given the lack of a specific and substantial well established utility for the claimed protein of SEQ ID No: 2, the rejection of claims under 35 USC 101 is maintained for the reasons of record.

Moreover, because the instant claims lack a specific and substantially well established utility, one of skill in the art would also not be able to make or use the

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invention. Therefore the rejection of the claims under 35 USC 112 1st paragraph is also maintained.

New Rejections

Claim Rejections - 35 USC § 112, 1st paragraph

5. Claims 6, 15, and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to an isolated peptide of SEQ ID No: 2 and to a method of detecting angiogenesis in a sample comprising the detection of the peptide of SEQ ID No: 2. The invention is in a class of invention which the CAFC has characterized as

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"the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art

The art teaches that mRNA levels are, as a general rule, are not indicative of enhanced levels of the encoded protein. For example, the textbook Genes VI (1997) by Benjamin Lewin points out that control of gene expression can occur at multiple stages and that production of RNA cannot inevitably be equated with the production of protein. More recently, Greenbaum *et al.* (Genome Biology, 2003, Vol. 4, Issue 9, pages 117.1-117.8) cautions against assuming that mRNA levels are generally correlative of protein levels. The reference teaches (page 117.3, 2nd column) that primarily because of a limited ability to measure protein abundances, researchers have tried to find correlations between mRNA and the limited protein expression data, in the hope that they could determine protein abundance levels from the more copious and technically easier mRNA experiments. To date, however, there have been only a handful of efforts to find correlations between mRNA and protein expression levels, most notably in human cancers and yeast cells. And, for the most part, they have reported only minimal and/or limited correlations. The reference further teaches (page 117.4, 2nd column) that there are presumably at least three reasons for the poor correlations generally reported in the literature between the level of mRNA and the level of protein, and these may not be mutually exclusive. First, there are many complicated and varied post-transcriptional mechanisms involved in turning mRNA into protein that are not yet sufficiently well defined to be able to compute protein concentrations from mRNA; second, proteins may

differ substantially in their *in vivo* half lives; and/or third, there is a significant amount of error and noise in both protein and mRNA experiments that limit our ability to get a clear picture. The reference further notes (page 117.6, page 2nd column) that to be fully able to understand the relationship between mRNA and protein abundances, the dynamic processes involved in protein synthesis and degradation have to be better understood. Hence, due to the teachings above, it would appear that production of mRNA, as a general rule, would not inevitably be predictive of equivalent levels of protein.

Working examples

The working examples of the instant invention are prophetic embodiments of the claimed invention. The specification does not provided any working examples for the use of the claimed polypeptide as a diagnostic tool nor does the specification provided any working method of detecting a polypeptide using an antibody that specifically reacts with SEQ ID No: 2.

Guidance in the specification

The specification provides little guidance for one of skill in the art for the use of the protein as a diagnostic marker and further fails to provide sufficient guidance for the method of detecting the peptide for the purposes of detecting angiogenesis.

Level of skill in the art

The level of skill in the art is deemed to be high.

Conclusion

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these

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unpredictable variables, the lack of guidance provided in the specification, the presence of a working example which does not address the issue of the efficacy of the control and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

All other rejections are withdrawn in view of the applicant's amendments and arguments thereto as set forth in a paper filed 2/14/2006.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H. Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen^{sen}
Art Unit 1643
March 3, 2006


CHRISTOPHER YAEN
PATENT EXAMINER